ethylmalonic encephalopathy

Ethylmalonic encephalopathy is an inherited disorder that affects several body systems, particularly the nervous system. Neurologic signs and symptoms include progressively delayed development, weak muscle tone (hypotonia), seizures, and abnormal movements. The body's network of blood vessels (the vascular system) is also affected. Children with this disorder may experience rashes of tiny red spots (petechiae) caused by bleeding under the skin and blue discoloration in the hands and feet due to reduced oxygen in the blood (acrocyanosis). Chronic diarrhea is another common feature of ethylmalonic encephalopathy.

The signs and symptoms of ethylmalonic encephalopathy are apparent at birth or begin in the first few months of life. Problems with the nervous system typically worsen over time, and most affected individuals survive only into early childhood. A few children with a milder, chronic form of this disorder have been reported.

Frequency

About 30 individuals with this condition have been identified worldwide, mostly in Mediterranean and Arab populations. Although ethylmalonic encephalopathy appears to be very rare, researchers suggest that some cases have been misdiagnosed as other neurologic disorders.

Genetic Changes

Mutations in the *ETHE1* gene cause ethylmalonic encephalopathy.

The *ETHE1* gene provides instructions for making an enzyme that plays an important role in energy production. It is active in mitochondria, which are the energy-producing centers within cells. Little is known about the enzyme's exact function, however.

Mutations in the *ETHE1* gene lead to the production of a nonfunctional version of the enzyme or prevent any enzyme from being made. A lack of the ETHE1 enzyme impairs the body's ability to make energy in mitochondria. Additionally, a loss of this enzyme allows potentially toxic compounds, including ethylmalonic acid and lactic acid, to build up in the body. Excess amounts of these compounds can be detected in urine. It remains unclear how a loss of the ETHE1 enzyme leads to progressive brain dysfunction and the other features of ethylmalonic encephalopathy.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal

recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- EME
- Encephalopathy, petechiae, and ethylmalonic aciduria
- EPEMA syndrome

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Elevated C4 and C5 +/- Other Acylcarnitines
  https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/C4_C5.pdf

Genetic Testing

- Genetic Testing Registry: Ethylmalonic encephalopathy
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1865349/

Other Diagnosis and Management Resources

- Baby's First Test
  http://www.babysfirsttest.org/newborn-screening/conditions/ethylmalonic-encephalopathy
- MedlinePlus Encyclopedia: Skin discoloration - bluish
  https://medlineplus.gov/ency/article/003215.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Skin discoloration - bluish
  https://medlineplus.gov/ency/article/003215.htm
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
- Health Topic: Mitochondrial Diseases
  https://medlineplus.gov/mitochondrialdiseases.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- Ethylmalonic encephalopathy
  https://rarediseases.info.nih.gov/diseases/2198/ethylmalonic-encephalopathy

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke
  https://www.ninds.nih.gov/Disorders/All-Disorders/Encephalopathy-Information-Page

Educational Resources

- Disease InfoSearch: Ethylmalonic Encephalopathy
  http://www.diseaseinfosearch.org/Ethylmalonic+Encephalopathy/2662
- MalaCards: ethylmalonic encephalopathy
  http://www.malacards.org/card/ethylmalonic_encephalopathy
- Orphanet: Ethylmalonic encephalopathy
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=51188

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases (CLIMB) (UK)
  http://www.climb.org.uk/
- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/metaboli.html

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28ethylmalonic+encephalopathy%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- ENCEPHALOPATHY, ETHYLMALONIC
  http://omim.org/entry/602473

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